

REMARKS

Claims 1 – 5, 9, 10, 12-14, and 16-23 are pending and under consideration. With this Amendment, claims 1, 9, 10 and 16 are amended, claim 23 is cancelled, and no new claims are added. Thus, after entry of this Amendment, claims 1 – 5, 9 – 10, 12 – 14, and 16 – 22 are pending and under consideration. The amendments to the claims and specification and the various rejections raised in the Office Action are discussed in more detail, below.

The Amendments to the Claims

Claim 1 has been amended to recite methods of treating clinical disorders that more closely parallel applicants' experimental model, clarifying that the clinical indication to be treated is a disorder of **trigeminovascular activation**. Written description support for this amendment can be found in the specification particularly at p. 13, lines 12 – 18 and 19 – 22. Consequential amendments have been made to claim 9, which depends from claim 1. Claim 10, which depends from claim 9, has been amended to limit the treated disorder to migraine with visual aura.

No new matter has been added by virtue of these amendments.

Rejections under 35 USC §§ 102 and 103

Claims 1 – 4, 9 – 10, 12, 13, and 19 – 22 stand rejected under 35 U.S.C. § 102(b) as anticipated by Pevarello *et al.*, WO 99/35125 (“the Pevarello PCT publication”). Although claims 5, 14, and 16 – 18, and 23 are free of rejection under 35 U.S.C. § 102, these latter claims are separately rejected as having been obvious over the Pevarello PCT publication under 35 U.S.C. § 103. The rejections have been obviated by amendment and should be withdrawn.

Claim 1, the sole independent claim in this application, has been amended particularly to claim methods of treating disorders of trigeminovascular activation. As amended, the clinical indications to be treated closely parallel applicants' experimental model, in which

[t]he above defined α -aminoamides have been found to be active in inhibiting cerebral **vasodilatation evoked by electrical stimulation of [the]** ophthalmic branch of rat **trigeminal ganglion**,

specification, p. 13, lines 19 – 22 (emphasis added). This animal model is accepted in the art as predicting efficacy in treating disorders of trigeminovascular activation, notably migraine, since

during the headache phase of migraine, a dilatation of both large extra[-] and intracranial arteries occurs. This event has been associated . . . [with] an antidromic **activation** with a consequent vasoactive neuropeptides release, and to an orthodromic **activation of the trigeminal fibers** associated with an increased neuronal activity”) (emphasis added).

Specification p. 13, lines 12 – 18 (emphasis added).¹ As herein amended, applicants’ claims are neither anticipated nor rendered obvious by the Pevarello PCT publication.

The Pevarello PCT publication describes the use of alpha-aminoamide compounds in the treatment of pain. The experimental model used to test these compounds – the formalin test – was well-accepted in the art, at the time the Pevarello PCT application and its priority application were filed, as reasonably predicting efficacy in treating acute and chronic pain having a wide range of etiologies. *See, e.g.,* Tjolsen *et al.*, “The formalin test: an evaluation of the method,” *Pain* 51:5-17 (1992) and Shibata *et al.*, “Modified formalin test: characteristic biphasic pain response,” *Pain* 38:347-352 (1989), of record herein respectively as items C50 and C43. Accordingly, the claims as issued in the U.S. counterpart of the Pevarello PCT publication, RE40,259, are broadly enabled as to “method[s] of treating acute or chronic pain in a patient in need thereof, said method comprising administering . . . an analgesically effective amount of an alpha-aminoamide compound” described by the formula thereafter recited. ‘259 Reissue, claim 1. *See, Rasmusson v. SmithKlineBeecham*, 413 F.3d 1318, 75 U.S.P.Q.2d 1297 (Fed. Cir. 2005); *In re Novak*, 306 F.2d 924, 134 U.S.P.Q. 335 (CCPA 1962) (quoted with approval in *Rasmusson*).

Prior to the amendments made herein, applicants’ claims had been drawn to methods of “treating head pain conditions.” As the Examiner recognized in the outstanding office action, the

¹ *See also* Pietrobon *et al.*, “Neurobiology of Migraine,” *Nature Reviews Neurobiology* 4:386-398 (May 2003), filed concurrently herewith in applicants’ supplemental information disclosure statement (IDS) as item C59 (particularly noting that “[a]ctivation of the trigeminovascular system is a central step in the development of migraine”), and Bolay *et al.*, “Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model,” *Nature Med.* 8:136-142 (2002), filed concurrently herewith in applicants’ supplemental IDS as item C60.

formalin test data in the Pevarello PCT publication (and '259 Reissue) would have been accepted by those of ordinary skill in the art as reasonably predicting that the alpha-aminoamide compounds described therein would be effective in treating acute or chronic head pain and on that basis, rejected all of applicants' then-pending claims.

The rejection has been obviated by amendment. Applicants now claim methods of "treating disorders of trigeminovascular activation." Although head pain is often a symptom of such disorders, and relief of head pain symptoms is within the scope of the Pevarello PCT teachings and the '259 reissue claims, relief of a symptom (head pain) neither anticipates nor here renders obvious treatment of the underlying disorder, as now distinctly claimed. As noted in applicants' last response and here reaffirmed, "the treatment of the underlying etiology is not synonymous with 'treatment of head pain,' any more than treatment of cardiac ischemia is synonymous with treatment of chest pain, or treatment of bone cancer is synonymous with treatment of bone pain."

Request for interview

Applicants respectfully request that the Examiner call the undersigned to schedule a personal interview if the Examiner believes that there are any matters outstanding that preclude issuance of the present claims.

Conclusion

Claims 1 – 5, 9 – 10, 12 – 14, and 16 – 22 are pending and under consideration. The claims as herein amended are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested. No fees beyond those due for extension of time are believed to be due in connection with this Amendment. However, the Director is authorized to charge any additional fees that may required, or credit any overpayment, to Dechert LLP Deposit Account No. 50-2778 (**Order No. 373987-004US (396982)**).

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Respectfully submitted,



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